IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Bradley Teegarden, *et al.*	Art Unit	: 1626
Serial No.	: 10/540,650	Examiner	: Shawquia Young
Filed	: April 21, 2006	Conf. No.	: 5391
Title	: DIARYLAMINE AND ARYLHETEROARYLAMINE PYRAZOLE DERIVATIVES AS MODULATORS OF 5HT2A		

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Commissioner for Patents
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PETITION FROM A RESTRICTION REQUIREMENT

The applicants hereby petition the Director under 37 C.F.R. §§ 1.144 and 1.181 to review the requirement for restriction and an objection related thereto made in the above-captioned application.

I. Statement of Facts

The above-captioned application was filed under 35 U.S.C. § 371 on April 21, 2006.

The application is directed generally to diarylamine and arylheteroarylamine pyrazole derivatives useful as modulators of the 5HT2A receptor. Claims 1-97 were pending in the International Phase. The claims were preliminarily amended upon entry to the National Phase. Claims 1-97 were cancelled and replaced by claims 98-122.

In an Office Action mailed on August 30, 2007, the Examiner required restriction under 35 U.S.C. § 121 among ten groups of allegedly independent and distinct inventions, which the Examiner characterized as follows:

> **Group I** claim(s) 98-117 (in part), drawn to a compound of formula (A) wherein: R_1 is phenyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 548.

Group II claim(s) 98-117 (in part), drawn to a compound of formula (A) wherein: R_1 is furanyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 548.

Group III claim(s) 98-117 (in part), drawn to a compound of formula (A) wherein: R_1 is thienyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 548.

Group IV claim(s) 98-117 (in part), drawn to a compound of formula (A) wherein: R_1 is pyridyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 546.

Group V claim(s) 98-117 (in part), drawn to a compound of formula (A) wherein: R_1 is pyrimidyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 544.

Group VI claim(s) 118-122 (in part), drawn to a method of use for a compound of formula (A) wherein: R_1 is phenyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-}

$_6$ alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 514.

Group VII claim(s) 118-122 (in part), are drawn to a method of use for a compound of formula (A) wherein: R_1 is furanyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 514.

Group VIII claim(s) 118-122 (in part), drawn to a method of use for a compound of formula (A) wherein: R_1 is thienyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 514.

Group IX claim(s) 118-122 (in part), drawn to a method of use for a compound of formula (A) wherein: R_1 is pyridyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98 excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 514.

Group X claim(s) 118-122 (in part), drawn to a method of use for a compound of formula (A) wherein: R_1 is pyrimidyl; R_2 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-7} cycloalkyl; R_3 is as defined in claim 98 excluding heteroaryl; R_{3a} is as defined in claim 98; R_4, R_{4a}, R_5, R_{5a}, are each as defined in claim 98

> excluding 5 or 6 membered-heteroaryl; R_6 and R_7 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group; wherein each said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, phenyl and benzyl group is optionally substituted with 1 to 5 substituents selected independently from the group as defined in claim 98, classified in various subclasses in class 514.

Office Action mailed August 30, 2007 p. 3-7.

The Office Action stated that the listing provided was "exemplary" and "not exhausted (*sic*)". *Id.* at 3 and 7. The Office offered the applicants, as an alternative to electing one of the groups, the option of electing a specific compound. *Id.* at 7.

In a response filed on February 28, 2008, the applicants elected Group I, but traversed and requested reconsideration of the restriction requirement. The applicants explained in detail some of the reasons that the restriction requirement was improper. Specifically, the applicants pointed out that the restriction requirement was improper at least because: (1) the Examiner failed to demonstrate that the claims lacked unity of invention; (2) the Groups from which election was required were arbitrary and improper; (3) no undue burden of searching the entire scope of the invention was established; (4) the restriction requirement was incomplete; and (5) the restriction requirement was unclear.

On June 19, 2008, a further Office Action was issued. The Examiner maintained the restriction requirement and made it final. Office Action mailed June 19, 2008, p. 5. The Office Action also contained an objection to certain subject matter as being non-elected, stating that the applicants "should submit an amendment deleting the nonelected subject matter". *Id.* at 9.

The applicants are filing a response to the Office Action of June 19, 2008 herewith.

II. Points to be Reviewed

The Director is respectfully requested to review whether the restriction requirement made by the Examiner in the Office Action mailed on August 30, 2007 was proper.

The Director is also respectfully requested to review whether the grouping of the restriction requirement, and whether the grouping would impermissibly exclude from examination subject matter sharing unity of invention with applicants' elected groups.

The Director is also respectfully requested to review the propriety of the objection to certain subject matter as being non-elected made in the Office Action dated June 19, 2008 and whether the applicants may be required to "submit an amendment deleting the nonelected subject matter."

III. The Action Requested

If the Director agrees with the applicants that the restriction requirement was improper, the Director is respectfully requested to require that the restriction requirement be withdrawn.

Even the Director agrees with the Examiner that a restriction requirement would have been proper in the application, the applicants nevertheless respectfully request that the Director review the arbitrary grouping of the claims and require rejoinder insofar as subject matter presently withdrawn from consideration sharing unity of invention with the applicants' elected group.

If the Director agrees with the applicants that the restriction requirement was improper, or that the requirement to "submit an amendment deleting the nonelected subject matter" was otherwise improper, the Director is also respectfully requested to require that the objection and requirement made in the Office Action dated June 19, 2008 therein be withdrawn.

IV. Arguments

A. Applicants are Entitled to Petition from the Restriction Requirement

An applicant may petition from a final requirement for restriction if reconsideration of the requirement was requested. 37 C.F.R. § 1.144.

Since the applicants requested reconsideration of the restriction requirement in their response filed March 4, 2008, specifically pointing out the errors in the restriction requirement

and the restriction requirement was made final in the Office Action mailed June 19, 2008, the applicants are now entitled to petition from the requirement for restriction.

B. The Restriction Requirement Made by the Examiner was Improper

Requiring restriction among Groups I-X was improper for at least the following reasons: (1) the Examiner failed to demonstrate that the claims lacked unity of invention; (2) the Groups from which election was required were arbitrary and improper; (3) no undue burden of searching the entire scope of the invention was established; (4) the restriction requirement was incomplete; and (5) the restriction requirement was unclear.

(1) Unity of Invention

The restriction requirement stated that unity is lacking because the inventions of Groups I-X were allegedly not so linked as to form a single general inventive concept under P.C.T. Rule 13. It was unclear how this conclusion was drawn, however because the Office did not analyze whether these groups share the same or corresponding special technical features. The compounds of formula (A) as defined in claim 98 did, in fact, share substantial common structural features which should have been found sufficient to establish unity of invention of claims 98-122 under P.C.T. Rule 13.

(a) The Applicable Legal Standard for Unity of Invention

"Unity of invention (not restriction) practice is applicable in ... national stage applications submitted under 35 U.S.C. 371." MPEP 1893.03(d). Unity of invention must be determined under the provisions of the P.C.T. in a national stage application filed under 35 U.S.C. § 371. *Caterpillar Tractor Co. v. Com'r Pat. & Trademarks*, 650 F.Supp. 218, 220 (E.D. Va. 1986). Therefore the legal standards applicable to making a restriction requirement in an application filed under 35 U.S.C. § 371 are those set forth for determining unity of invention under the P.C.T. as given in the P.C.T. itself and the P.C.T. rules (specifically Rule 13).

The standard for unity of invention under the P.C.T. as set forth in P.C.T. Rule 13, states:

> the requirement of unity of invention ... shall be fulfilled ... when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

P.C.T. Rule 13.2. Unity of invention is satisfied when there is a special technical feature linking the claims. The presence of a special technical feature linking the claims thus defines the unity of invention standard.

While the combination of features defining a "special technical feature" under the P.C.T. must define a contribution over the prior art, the prior art which is to be considered for the purpose of determining unity of invention must have been published prior to the international filing date of the application. Unity of invention is determined under the P.C.T. and the P.C.T. rules, specifically Rule 13. *See Caterpillar Tractor Co.*, 650 F.Supp. at 220. Although Rule 13 itself does not expressly explain what qualifies as "prior art" for the purposes of determining unity of invention, it is clear that what is "prior art" must be determined under the P.C.T. rules. The only clear definition of what qualifies as "prior art" in the P.C.T. Rules elsewhere define the "relevant prior art" as that which has been published prior to the international filing date, and the P.C.T. rules do not suggest that a different standard should be applied in considering unity of invention. Rule 33.1 defines the relevant prior art for the purposes of Article 15(2) as "everything which has been made available to the public anywhere in the world by means of written disclosure ... *provided that the making available to the public occurred prior to the international filing date.*" P.C.T. Rule 33.1 (emphasis added). Rule 33.1(c) specifically indicates that applications filed or having an earlier priority date but published later than the application being examined is not such "relevant prior art" (but rather is art that ***would*** constitute relevant prior art "***had it been published prior*** to the international filing date." (emphasis added)) Patent applications which are unpublished as of the international filing date therefore are clearly not considered "prior art" under the P.C.T. rules and do not qualify as prior art for the purpose of determining unity of invention.

Authoritative guidelines for determining whether there is unity of invention in specific situations are provided in the Annex B to the Administrative Instructions under the P.C.T. (the

"Administrative Instructions") and also in Chapter 10 of the P.C.T. International Search and Preliminary Examination Guidelines (the "Preliminary Examination Guidelines").

Particular standards set forth in these guidelines that are relevant to unity of invention in the present application are discussed in greater detail below.

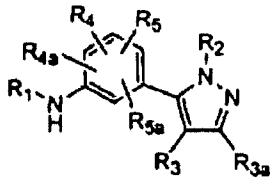
First, where there is unity of invention within and among independent claims, there is also unity of invention among dependent claims. The Administrative Instructions explain that unity of invention should be considered first in relation to the independent claims. Then, "[i]f the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims" Administrative Instructions under the P.C.T. Annex B, para. (c)(i).

Second, there is unity of invention as between a claims to a product, and claims to methods of making and using the product. The Administrative Instructions explain that the standard for unity of invention under Rule 13.2 should be construed as permitting "in addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product." Administrative Instructions under the P.C.T. Annex B, para. (c)(i).

Third, the Administrative Instructions establish that when a series of chemical compounds is defined in a claim using so-called "Markush practice" enumerating alternative elements, "[t]he fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for a finding of a lack of unity of invention." Administrative Instructions under the P.C.T. Annex B, para. (f)(iv). Unity of invention is satisfied when a significant structural element is shared by all of the alternatives. The significant structural element may be a single component or a combination of individual structural elements linked together. Administrative Instructions under the P.C.T. Annex B, para. (f).

(b) The Common Features of the Compounds of Formula (A) as Defined in Claim 98 Constitute Special Technical Features Linking the Claims

The Examiner's only reasoning justifying the restriction requirement was as follows:

> The claims herein lack unity of invention under PCT Rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art (See, WO 2004/046118 A2, for example).
>
> The compounds claimed contain  , which does not define a contribution over the prior art. The compounds vary in classification and when taken as a whole result in vastly different compounds. Accordingly, the vastness of the claimed subject matter and the complications in understanding the claimed subject matter imposes a burden on any examination of the claimed subject matter.

Office Action mailed August 30, 2007 beginning at p. 7 line 22.

As the applicants pointed out in traversing the restriction requirement, it is the presence of a special technical feature, and not the diversity of the compounds sharing that feature, which determines whether there is unity of invention within and among claims directed to a family of chemical compounds. The claims can have unity of invention even though the compounds claimed therein might have variable substituents, encompass a diversity of compounds and vary in classification, so the Examiner erred in considering only these factors, which were, in fact, largely irrelevant to the issue of unity of invention.

Since claims 99-122 all depend from claim 98, unity of invention among all the claims depends on whether there is unity of invention within claim 98. The Administrative Instructions under the P.C.T. explain that "[i]f the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims" Administrative Instructions under the P.C.T. Annex B, para. (c)(i).

When the independent claims of the application were considered, the Examiner should have recognized that the compounds of formula (A) as defined in claim 98 (Figure 1) in fact have numerous common features sufficient to constitute a special technical feature.

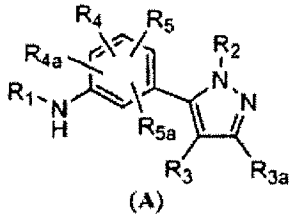


Figure 1. Common Structural Features of the Compounds According to Formula (A).

The common features of the compounds of formula (A) as defined in claim 98 include, for example:

- a phenyl ring substituted by an amino group (R_1NH) and a pyrazole ring;
- the R_1NH amino group and pyrazole ring substituting the phenyl group are in a 1,3-relationship relative to each other;
- the amino group is substituted by a second aromatic ring (R_1) optionally substituted with a limited range of substituents as described in the definition of R_1;
- the pyrazole ring is attached to the phenyl ring at the 5-position; and
- the pyrazole ring has an aliphatic hydrocarbon substituent (R_2) at the 1-position.[1]

These common features may be represented by the following substantial common substructure of all the compounds according to formula (A) (where * represents points of attachment of optional substituents represented by substituents R_3, R_{3a}, R_4, R_{4a}, R_5, and R_{5a}:

[1] In describing the numbering of the pyrazole ring positions here, the applicants number the ring atoms of the pyrazole ring beginning on the nitrogen bearing the substituent as the 1-position, proceeding to the second nitrogen as the 2-position.

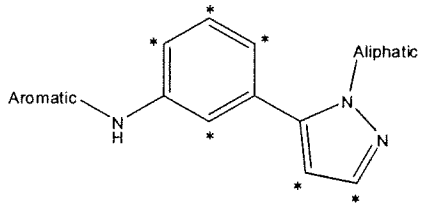


Figure 2. Common Structural Features of the Compounds According to Formula (A).

The different definitions of R_1 in Groups I-V do not establish lack of unity of invention. The principal difference between compounds of Groups I-V is in the definition of R_1 as phenyl, furanyl, thienyl, pyridyl, or pyrimidinyl. All of these groups (furanyl, thienyl, pyridyl, or pyrimidinyl as well as all of the possible options for R_1 in Formula A as defined in claim 98) belong to a recognized class, namely aromatic rings. The art recognizes aromatic rings as a single class of chemical moiety, which includes both carbocyclic and heterocyclic rings, and encompasses conjugated unsaturated ring systems having 4n+2 pi electrons. The WIPO guidelines point out that the possibility that the alternatives of a Markush group *could* be differently classified is not sufficient justification for a finding of lack of unity of invention. The fact that options available for R_1 include phenyl, furanyl, thienyl, pyridyl, or pyrimidinyl etc., which *could* be separately classified, therefore does not defeat unity of invention. All of these options for R_1, although capable of being differently classified, nevertheless belong to the art recognized class of aromatic rings.

The arbitrary exclusion of heteroaryl groups from the definitions of R_3, R_4, R_{4a}, R_5, and R_{5a} in the Examiner's definitions of each of Groups I-V (e.g. "R_3 is as defined in claim 98 *excluding heteroaryl*") also was not related to whether the inclusion of heteroaryl groups in these definitions would establish lack of unity of invention. The common sub-structural features of the compounds according to Formula A constitutes a special technical feature without regard to whether the variable substituents R_3, R_4, R_{4a}, R_5, and R_{5a} might encompass heteroaryl groups.

Although the applicants recognize that the nature of the patent classification system might make it *convenient* for the Office to separate the searches of Groups of compounds having different heterocyclic systems (as reflected in the different heterocyclic rings defined for R_1 in Groups I to V) (since different heterocyclic systems are differently classified), a restriction in an

application in a National Phase application filed under 35 U.S.C. § 371 must be based upon a proper finding of lack of unity of invention under the P.C.T. rather than an arbitrary division of applicants' claims according to what might be convenient for the Office to search.

The court in *In re Harnisch,* 631 F.2d 716 (CCPA 1980) applied the standard of unity of invention in relation to the propriety of a restriction requirement in a domestic application. Unity of invention was held to exist where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility. MPEP 803.02. The claims to the compounds claim 98 clearly meet the unity of invention standard as defined in *Harnisch*, at least because:

(1) the compounds share the *common utility* of modulating the activity of the $5HT_{2A}$ receptor;

(2) the compounds *share a substantial structural feature* as defined above;

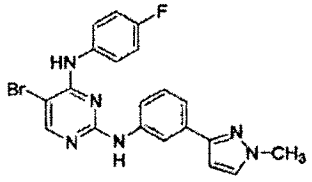
(3) the structure of the compounds as defined in formula I will be understood to be *essential to the utility* of the compounds because it is well known that biological activity of pharmaceutical compounds is a result of the molecular interaction between the compounds and the biological macromolecules that are the effectors of the biological response, and hence dependent on the molecular structure of the compounds.

The applicants further point out that the substituents R_1-R_6, are variable substituents attached to the core which represents a common structural feature in much the same way that the claim at issue in *Harnisch* defined variable substituents attached to a common core and therefore the fact that these substituents may be variable does not detract from the fact that the claims to the compounds according to formula (A) comply with the unity of invention requirement.

Although the Office Action cited WO2004/046118 to support its contention that the claims lack unity of invention, the Examiner did not explain *how* it was supposed that the reference cited defeated unity of invention.

WO04/046118 was cited without any explanation of how it was supposed that the reference defeated unity of invention, although it was implied that the reference somehow prevented the compounds of formula (A) from defining a contribution over the prior art. Office

Action mailed August 30, 2007 beginning at p. 8 lines 1-2. Despite the applicants pointing to the lack of an adequate explanation (Reply filed March 4, 2008, p. 10, second paragraph), no further explanation has been provided in the most recent Office Action, which merely refers back to the prior Office Action. Office Action mailed June 19, 2008, p. 3 lines 8-10. The Examiner placed into the record, and provided the applicants, with the cover page and p. 106 of WO04/046118. Page 106 of WO04/046118 describes the preparation of the following compound:



A prior art reference describing a particular feature of the claims may establish that such a feature does not qualify as a special technical feature because of the failure of the feature define a contribution over the prior art. The record, however, does not establish that the common features of the compounds of formula (A) as defined in claim 98 and described above do not define a contribution over the prior art.

First, WO04/046118 is *not prior art* to the present application for the purposes of determining unity of invention over the present application,[2] and therefore would not defeat unity of invention even described the applicants' special technical feature. The present application is the National Stage Entry of PCT/US03/40844, which has an international filing date of December 22, 2003. The cover of WO04/046118 shows that it was published on June 4, 2004, *later than the international filing date* of the present application. Unity of invention in a P.C.T. National Phase application is determined by reference to the P.C.T. Rules. As the applicants pointed out above, the P.C.T. Rules elsewhere define the "relevant prior art" as that which has been published prior to the international filing date. Since WO04/046118 was filed later than the international filing date of the present application, the reference is not prior art for the purposes of determining unity of invention, and therefore cannot be used to defeat unity of invention.

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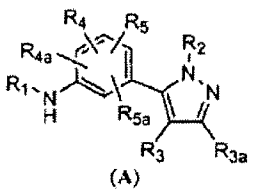
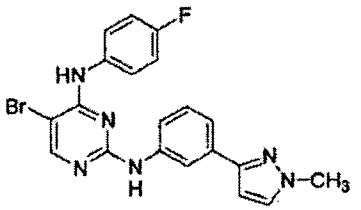
[2] Whether the reference could be prior art for the purpose of determining patentability under U.S. law, for example under 35 U.S.C. § 102(e), is irrelevant to whether the reference qualifies as prior art for the purposes of determining unity of invention. Unity of invention is determined under the provisions of the P.C.T. and the P.C.T. rules, and not under the provisions of the U.S. patent law. Section 102 is not part of the P.C.T. or the P.C.T. Rules.

Second, even if WO04/046118 were prior art for determining unity of invention, the record established by the Examiner in support of the restriction requirement does not demonstrate that the reference describes the features of the compounds of formula (A) as defined in claim 98. The examiner did not explain how WO04/046118 discloses the common features of the compounds of formula (A) as defined in claim 98. Although the Examiner placed p. 106 of the reference in the record and provided a copy of the same page to the applicants, it must be acknowledged that the compound on p. 106 of the reference clearly does not show the features which are common to the compounds of formula (A), as is evident if the structures are compared side-by-side:



Formula (A).



Compound from p. 106 of WO04/046118

From this comparison, it is clear that the compound from p. 106 of WO04/046118 does not show all the features common to the compounds of Formula (A) of claim 98, because:

(1) Referring to the definitions of claim 98, it will be seen that R_2 is always an aliphatic substituent. The compounds of formula (A) of claim 98 always have an aliphatic substituent at 1-position of the pyrazole ring, while the phenyl ring (which bears R_4, R_{4a}, R_5, R_{5a}, and NHR_1) is at the adjacent 5-position of the phenyl ring. In contrast, the methyl group and benzene ring are in completely different relative positions as substituents of the pyrazole ring of the compound on p. 106 of WO04/046118: if the methyl group is regarded as being at the 1-position, the phenyl group is at the non-adjacent 3-position.[3] This is not the same disposition of the substituents as is found in the compounds of formula (A).

(2) Furthermore, the compound above from WO04/046118 does not have a group corresponding to R_1 on the compounds of formula (A) because R_1 on the compounds of formula

[3] The same numbering system as described in footnote 1 is used, where the ring atoms of the pyrazole ring beginning on the nitrogen bearing the substituent as the 1-position, proceeding to the second nitrogen as the 2-position.

(A) may not be aryl or heteroaryl further substituted by an arylamino according to the definitions in claim 1.

Based on the foregoing, there is nothing in the record that establishes lack of unity of invention. First, the compounds of formula (A) of claim 98 are a feature common to all the claims, and clearly have substantial common structural features. The Examiner has made no showing that these common features do not represent an advance over to the relevant prior art.

(c) The Use Claims 118-122 Share Unity of Invention with Compound Claims 98-117 Based upon the Common Features of the Compounds According to Formula A as a Special Technical Feature and the Dependency of these Claims

The restriction requirement made was also inconsistent with the standards for unity of invention under the P.C.T. and improper insofar as restriction was required among claims to compounds and compositions (in Groups I-V) and methods of using these compounds (in Groups VI-X). The novel compounds clearly constitute a special technical feature linking the claims to the compounds with the claims to methods for their use.

The impropriety of the division of the method of use claims 118-122 from the compound claims of claims 98-117 is apparent from at least two of the guidelines for the determination of unity of invention provided in the Annex B to the Administrative Instructions under the P.C.T. (the "Administrative Instructions"):

(1) Unity of invention is apparent from the dependency of claims 118-122 from claim 98. The Administrative Instructions explain that "[i]f the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims" Administrative Instructions under the P.C.T. Annex B, para. (c)(i).

(2) Unity of invention is also apparent because claims 98-117 and claims 118-122 are related as claims to a product, and claims to methods using the product. The Administrative Instructions explain that the standard for unity of invention under Rule 13.2 permits "in addition to an independent claim for a given product ... an independent

claim for a use of the said product." Administrative Instructions under the P.C.T. Annex B, para. (c)(i).

The applicants respectfully point out that even if the Examiner were correct as to lack of unity among Groups I-V, for example, the division of Groups VI-X from the corresponding compound claims was improper. For example, compounds in Group I are a shared common feature among the compound claims of Group I and the method claims of Group VI. Even if, as alleged by the Office, the requirement of unity of invention were not fulfilled among all of Groups I to X, the requirement would certainly be met among Groups I and VI. Therefore, even if the restriction requirement were deemed otherwise proper, the subject matter of Group VI should be rejoined.

(2) Even If a Lack of Unity of Invention Were Established, the Groups From Among Which Election Was Required Were Arbitrary and Improper

(a) The Restriction Requirement Has Abridged The Applicants' Right To Claim Generically the Subject Matter Which They Regard As Their Invention

35 U.S.C. § 121 gives the Office the right, "[i]f two or more independent and distinct inventions are claimed in one application [to] require the application to be restricted to one of the inventions." The right granted by 35 U.S.C. § 121 is therefore to require that an application be limited to one of the inventions *claimed by the applicants* in the application. Indeed, it is a statutory requirement that the claims of an application must describe "the subject matter *which the applicant regards* as his invention." 35 U.S.C. § 112. It is therefore up to the applicants, and not the Office, to define the metes and bounds of their claims.

The restriction requirement made in the present application, would, if maintained, exceed the authority granted to the Office by 35 U.S.C. § 121 and violate the applicants' right to claim what they regard as their invention by requiring the claims to be rewritten in a manner where generic terms the applicants have used in describing their invention would be required to be replaced by different terms having a different meaning. For example, the Examiner would apparently have the applicants substitute the generic definition of R_1 as "aryl or heteroaryl each

optionally substituted ..." by narrower definitions as *particular* aryl or heteroaryl rings, i.e. as phenyl, furanyl, thienyl, pyridyl or pyrimidinyl.

The right of the Office to insist upon restriction when an application claims more than one invention does not give the right for the Office rewrite the applicants' claims to an invention which the applicants have already properly claimed using *bona fide* generic terms. The fact that the claims might encompass more than one invention in the sense of dominating them is an insufficient reason for maintaining a restriction requirement where a generic claim encompasses more than one of the inventions. *See In re Weber*, 580 F.2d 455, 460 (C.C.P.A. 1978) (Rich J. concurring) (noting that "the obvious fact that almost any reasonably broad claim 'embraces' or 'covers' a multiplicity of inventions, in the sense of 'dominating them' ... is not a sufficient excuse for refusing to examine a claim on its merits for compliance with 35 U.S.C. §§ 101, 102, 103, and 112.") That the compounds of Groups I-V are dominated by claim 98 therefore does not detract from the fact that claim 98 properly claims applicants' invention in generic terms.

(b) The Arbitrary Definitions of the Groups Would Deprive the Applicants of Their Right To Claim The Entirety of Their Invention

A proper restriction requirement should encompass and account for all elements of the original claims, without any voids or ambiguities, so that applicants' entire claimed invention may eventually be examined. An applicant has a right to have each claim examined on the merits in its entirety. *In re Weber*, 580 F.2d 455 (CCPA 1978). The totality of any fragmentary claims must necessarily be the equivalent of the original claim. *Id.* at 458. The applicant has a right to claim his invention as he chooses, and this statutory right takes priority over perceived administrative needs. *Id.* at 459.

By splitting the compound claims in the manner required by the restriction requirement, the Examiner has created artificial genera that were different from those claimed in the application. The invention claimed in claim 98 (for example) was the compound wherein R_1 is "aryl or heteroaryl", and not a compound wherein "R_1 is selected from phenyl, furanyl, thienyl, pyridyl, and pyrimidinyl" as suggested by the restriction requirement. The invention claimed in claim 98 was also not a compound wherein heteroaryl groups are excluded from the definitions

of R_3, R_4, R_{4a}, R_5, and R_{5a}. If the applicants were required to pursue subject matter of their invention according to the division insisted upon by the Examiner, they would be forced to divide and reformulate the subject matter into multiple claims to comply with the restriction and written description requirements by canceling various subject matter. As a result, there could be no guarantee that the scope of the resulting fragments would necessarily equal the originally claimed scope, but rather might be marred with voids and ambiguities of potentially inaccessible subject matter. Accordingly, the applicants would have no choice but to forego rights to subject matter to which they are entitled. Forced forfeiture of rights resulting from the contrived and artificial delineation of the compound claims as specified in the Office action merely due to administrative conveniences is clearly beyond the bounds of the Office's statutory authority as discussed in *In re Weber*, supra.

(c) Even If Lack of Unity of Invention Were Established, The Arbitrary Definitions of the Groups Would Limit Applicants' Invention More Than Could Conceivably Be Required To Restore Unity of Invention

Even if unity of invention were found to be lacking as to one or more claims, the Office would not thereby given "carte blanche" under the P.C.T. to divide applicants' claims as it sees fit. Rather, 35 U.S.C. § 121 only authorizes the claims to be restricted to an invention claimed by the applicants.

Further, the applicants have the "right to include in a single application ... those inventions which are so linked as to form a single general inventive concept". MPEP 1893.03(d). Therefore even if a lack of unity of invention were to be established as to some of the claims, restriction is permissible only to the extent necessary to restore unity of invention. The applicants are entitled to retain in the application all of the subject matter sharing unity of invention with the applicants' elected group.

Focusing on the applicants' elected group, even if the Examiner were correct that the claims lacked of unity of invention, the requirement to maintain unity of invention would not justify why R_1 should be limited only to phenyl and not other carbocyclic aromatic groups within the definition of "aryl" as claimed in claim 98. The Examiner also did not explain why having

R_3, R_4, R_{4a}, R_5, and R_{5a} as heteroaryl groups would be inconsistent with unity of invention, and therefore the applicants should also be permitted to retain this subject matter. The Office also had no basis to require restriction between the compound and method of use claims from the compound claims, since claims to a product and method of its use share unity of invention under proper P.C.T. practice described above.

Therefore, even if the Director were to find that the Examiner were correct in finding lack of unity of invention, rejoinder of the wrongfully withdrawn subject matter should be required. The applicants expand upon this request in (C) below.

(3) Failure to Demonstrate Undue Burden

MPEP 803 explains that if the search and examination of all the claims in an application can be made without serious burden, the examiner must examine them on the merits, even though restriction might otherwise be proper. *See* MPEP 803.

The Examiner's contention that a search of all the products and methods would be unduly burdensome is not compelling. In view of the substantial structural similarities shared by all compounds according to formula (A), it would clearly not constitute an undue burden for the Examiner to search all of the claims together.

The applicant suggested in traversing the restriction requirement that the substantial sub-structure identified above could serve as the basis for a computational search in the Chemical Abstracts database, allowing the claimed inventions all to be searched together by the Examiner.

The Examiner's response to the applicants' traversal fails to indicate that the Examiner has given any serious consideration to the applicants' arguments. The Examiner could have addressed the applicants' suggestion, for example, by having a sample search of the CAS database performed based the common substructure of the compounds (which can be performed at minimal cost) to assess the feasibility of searching the applicants' claims.

Instead, the Examiner's response to the applicants' arguments states:

> However, the Examiner wants to point out that the compounds embraced by formula I are classified in different classes such as 544, 546, 548, etc. and

> consist of different inventions that are patentably distinct and independent. Therefore, different search considerations are involved (i.e., class/subclass searches, databases searches, etc.) for each of the inventions encompassed by group I. Each Class 514, 544, 546 and 548 encompasses numerous patents and published applications. For instance, Class 514 contained 165,171 patents and published applications. Therefore it would constitute a burden on the Examiner and the Patent Office's resources to examine the instant application in its entirety. As mentioned in the Restriction Requirement that "all compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election will be directed to nonelected subject matter and will be withdrawn from consideration under 35 USC 121 and 37 CFR 1.142(b)". Applicants did not traverse the restriction requirement.[4]

The Examiner's response does not indicate any serious consideration of applicants' suggestion that the entire claim could be searched together without undue burden using an automated computational search. Furthermore, all of Groups I-III were, in fact, commonly classified by the Examiner in Group 548, and therefore the Examiner's own explanation of the supposed burden of searching the entirety of the applicants' invention fails to account for the need to require restriction among Groups I-III.

Moreover, even if the Director were to find that the Examiner had, in fact, established that searching the entirety of the applicants claims would impose a substantial burden, the question of how much burden would be imposed by searching the applicants' claims in their entirety only arises once the Examiner has established that the claims lack unity of invention, which is not the case here.

(4) Incompleteness and Lack of Clarity of the Restriction Requirement

MPEP 815 explains that "[w]hen making a restriction requirement every effort should be made to have the requirement complete." It is apparent from the Office Action making the restriction requirement that the restriction requirement is not complete because the Office Action expressly states that not all of the inventions have been listed.

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[4] The applicants did, in fact, traverse the restriction requirement, and provided a thorough explanation of why it was believed to be improper.

MPEP 814 explains that making a restriction requirement, the Office must "provide a clear and detailed record of the restriction requirement to provide a clear demarcation between restricted inventions so that it can be determined whether inventions claimed in a continuing application are consonant with the restriction requirement and therefore subject to the prohibition against double patenting rejections under 35 U.S.C. 121." MPEP 814 (citing *Geneva Pharms. Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1381 (Fed. Cir. 2003).

The applicants pointed out that the restriction requirement was improper because it was incomplete, by virtue of omitting some of the inventions among which restriction was being required, and unclear by virtue of its incompleteness.

In response to the applicants' traversal, the Examiner responds that:

> The Examiner wants to emphasize that the claimed invention embraces vast subject matter and it would be impossible, with the limited time the Examiner is given to work on each case, to state all of the possible groups that are embraced by the formula I. As mentioned in the Restriction Requirement, the groups listed are only exemplary but not the only groups possible. The restriction requirement was not incomplete. In the situation of a 371 case, the Examiner has disclosed why the claimed invention lacks unity of invention and has listed some of the exemplary groups of the distinct and independent inventions embraced by the claimed invention in claim 98.

The Examiner's response therefore admits that the restriction requirement was incomplete and does not deny that it was unclear.

The applicants are not unsympathetic to the Examiner's predicament of being allowed a limited time to work on a given application, but the applicants do not believe any limitations imposed by the Office's practices in this regard are sufficient reasons for failing explain the restriction requirement completely and clearly.

Here, moreover, any problem the Examiner might have in making the restriction requirement complete and clear arise from the improper nature of the restriction requirement, in which the Examiner has sought to divide the claims to a far greater degree than could be justified to ensure claims having unity of invention using arbitrary and artificial groupings not based upon the claims. The applicants will face a similar dilemma to the Examiner if they are forced to

attempt recapture the entirety of their invention by filing divisional applications to the subject matter not included within the artificial Group constructed by the Examiner.

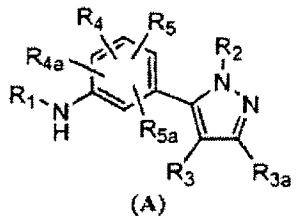
Even if the restriction requirement were otherwise proper, it would be important for the restriction requirement to be based on the claims, and for the applicants to have a clear and detailed record of the demarcation between the invention to which the present application may be restricted and any inventions which might be pursued in future divisional applications. Yet, the restriction requirement fails to provide the required definitions and clear demarcation.

C. Even if Making A Restriction Requirement Were Proper, The Applicants are Entitled To Rejoinder of Subject Matter Sharing Unity of Invention with the Elected Group.

Even if the Director agrees with the Examiner that the claims lacked unity of invention, the applicants request that the Director review the grouping of the subject matter of the claims in the restriction requirement, and whether the grouping would impermissibly exclude from examination subject matter sharing unity of invention with applicants' elected groups.

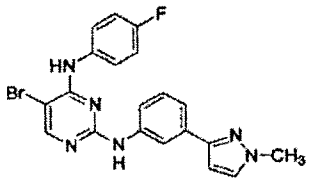
The applicants consider that even if the Director finds that the Examiner's finding of a lack unity of invention was correct, the Director should nevertheless find that the grouping was improper. As explained above, the applicants believe that the grouping is arbitrary, and would divide the claims to a far greater degree than would be necessary to restore unity of invention, based upon the record. Rejoinder of the wrongfully restricted and withdrawn subject matter should be required.

The applicants have pointed out that the common elements of the compounds of formula (A) constitute a special technical feature linking the groups and the claims:



(A)

The Examiner, on the other hand, has cited WO04/046118 as defeating unity of invention. Although the Examiner has not explained how WO04/046118 is supposed to defeat unity of invention, the Examiner provided applicants with a page from the application showing the following compound:



The applicants disagree that WO04/046118 defeats unity of invention.

Even if the Examiner's argument that WO04/046118 defeats unity of invention were accepted as correct, the reference does not justify restricting the applicants' application beyond limiting R_1 to *aryl*. Accepting the Examiner's arguments, the above compound from WO04/046118 would seem to correspond most closely to a compound of formula (A) with R_1 as *heteroaryl* (i.e. R_1 as pyrimidine, a heterocycle). The Examiner could not argue that the above compound WO04/046118 shows a compound corresponding to a compound of formula (A) with R_1 as *aryl*. No further limitation of the claims beyond limiting R_1 to *aryl* could therefore justified by any need restore unity of invention. To the extent that the definition of Group I further limits examination beyond limiting R_1 to *aryl* , the restriction requirement has wrongfully withdrawn from examination more subject matter than needed to restore unity of invention.

Since applicants are entitled to retain in the invention all "those inventions which are so linked as to form a single general inventive concept", *see* MPEP 1893.03(d), the Director should require rejoinder of the wrongfully withdrawn subject matter. Specifically, the restriction requirement should be modified to require rejoinder of at least all the compounds according to claim 1 in which R_1 is aryl. The Examiner has failed to explain why exclusion of carbocyclic aromatic groups other than phenyl in the definition of R^1 would be necessary to overcome lack of unity of invention. The Examiner has also failed to explain how the arbitrary limitations on the definitions of R_3, R_4, R_{4a}, R_5, R_{5a}, (exclusion of heteroaryl); and R_6 and R_7 (exclusion of embodiments wherein R_6 and R_7 together form a ring) are in any way related to the requirement of unity of invention.

The applicants also believe that the method claims insofar as they are directed to uses of the elected compounds, should also be rejoined since dependent claims directed to methods of using compounds necessarily share unity of invention with corresponding compound claims under proper P.C.T. unity of invention practice. The wholesale withdrawal of the method claims is improper under P.C.T. unity of invention practice because the common features of the compounds of the compound claims are also features of the method claims.

Based on the foregoing, the applicants submit that even if the Director was to find that the Examiner was correct in initially finding a lack of unity of invention, the Director should also find that the grouping insisted upon by the Examiner was improper. The Director should require rejoinder of all the subject matter of the claims insofar as they are directed to compounds according to claim 1 in which R_1 is aryl and methods of using such compounds.

D. The Objection to Non-Elected Subject Matter made in the Office Action dated June 19, 2008 and the Requirement that the Applicants Cancel Non-Elected Subject Matter Was Improper

In addition to maintaining the restriction requirement, the Office Action mailed June 19, 2008 included an objection to non-elected subject matter and a requirement that the applicants must "submit an amendment deleting the nonelected subject matter". Office Action mailed June 19, 2008 p. 9.

The objection and requirement made therein are improper because the restriction requirement is improper.

Moreover, the requirement is also improper because claim 98 is a linking claim linking the compounds of Groups I-V. Each of Groups I-V is an embodiment of, and is therefore a species of, the compounds claimed in Groups I-V. MPEP 809 clearly explains that a genus claim linking species claims counts as a linking claim.

Even if the Examiner was correct that they were otherwise properly divisible, encompassing more than one of the inventions, the objection would be improper because the linking claim is a part of the elected invention. While the Office may, under restriction practice,

initially limit the examination of claims encompassing more than one invention to the elected invention, unless a statutory basis for rejecting the claim is found, examination of the claim must be expanded to encompass additional inventions within the scope of the claim. There is no basis for the Office to object to, and refuse to examine, claims merely because they encompass more than one invention. *See In re Weber*, 580 F.2d 455, 460 (C.C.P.A. 1978) (Rich J. concurring).

Under 35 U.S.C. § 131 and 132, the Office is required to examine the claims and allow them if they meet the requirements of the statute, or to reject them if they do not. 35 U.S.C. § 121 allows the Office to withdraw from examination claims that are drawn to non-elected subject matter when inventions are independent and distinct.

The applicants are unaware of any provision in the statute, the Office's regulations, or the MPEP that permit an Examiner to refuse to examine and require the applicants to cancel part of a claim merely because a claim happens to dominate one or more otherwise divisible inventions. Indeed, MPEP 809 clearly explains that linking claims encompassing more than one Group of divided inventions **"must be examined with, and thus are considered part of, the invention elected."** The MPEP further indicates that "[w]hen all claims directed to the elected in invention are allowable, should any linking claim be allowable, the restriction requirement between the linked inventions must be withdrawn. Any claim(s) directed to the non-elected invention(s), previously withdrawn from consideration, which depends from or requires all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability." MPEP 809. MPEP 809 makes no mention of the possibility, instead, of objecting to such claims and asking the applicants to rewrite them to unlink the inventions.

Therefore, the MPEP indicates that when a restriction requirement is proper, but linking claims are present, although an initial restriction requirement might be made (if otherwise proper), upon finding the claims to the elected invention allowable, the Examiner must expand the examination to include other inventions. The Office Action mailed June 19, 2008, however, suggests that the Examiner does not propose to follow the procedure set forth in the MPEP, but rather would seek to require the applicants to delete the non-elected subject matter.

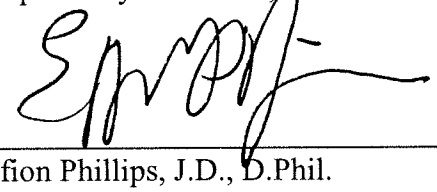
Based on the foregoing, the applicants request that the objection made in the Office Action dated June 19, 2008, and the requirement that the applicants must submit an amendment deleting the non-elected subject matter" be found to be improper.

E. Conclusion

For the reasons given above, the applicants respectfully ask the Director to **grant** this petition, and require that the restriction requirement made in the Office Action mailed August 30, 2007 be **withdrawn**.

No fee is believed to be due for filing this petition. If, however, any fee is due, please apply any charges or credits as appropriate to deposit account 06-1050 referencing Attorney's Docket No. 20750-0034US1 / 004.US3.PCT.

Respectfully submitted,



Date: 12/18/2008.

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